

**BIOGRAPHICAL SKETCH**

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NAME: Paolo Casali

eRA COMMONS USER NAME (credential, e.g., agency login): paolocasali

POSITION TITLE: Zachry Foundation Distinguished Professor and Chairman  
Department of Microbiology, Immunology & Molecular Genetics

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Milan, School of Medicine and Surgery, Milan, Italy 20122	M.D.	06/73	Medicine and Surgery
University of Milan, School of Medicine and Surgery, Milan, Italy 20122	<i>Cum Laude</i>	06/76	Allergy and Clinical Immunology
University of Milan, School of Medicine and Surgery, Milan, Italy 20122	Specialty and Board Specialty and Board	10/84	Microbiology and Virology
1973-1976	Medical Resident, Department of Internal Medicine, University of Milan, 20122 Milan, Italy.		
1976-1978	Doctorat en Immunologie, World Health Organization Immunology Research & Training Center, Département de <a href="#">Médecine</a> , Ecole de <a href="#">Médecine</a> , Université de Genève, 1211 Genève, Suisse.		
1978-1979	Medical Resident, Department of Internal Medicine, University of Milan, 20122 Milan, Italy.		

**A. Personal Statement**

My experience in and dedication to higher education and research in biomedicine lead convergently to support this application to mentor and train medical students from Central South University Xiangya School of Medicine in basic biomedical science research. In the last 10 years, I have mentored 12 Ph.D. students (three Ph.D. and one M.D./Ph.D. students currently in training) and 4 Master's students. Nine of the 10 students would have been eligible for this T32 support; the 10<sup>th</sup> was an international student) and 6 post-doctoral fellows (one currently in training). I have a strong record of mentorship and accomplishments in basic and translational science research. I was the director of the Graduate Program in Immunology at Cornell University Weill Medical College, for which I obtained the first NIH Training Grant in Immunology Research (NIH T32 AI 007621) in 2009 (currently in its third renewal). I left this T32 grant behind at Cornell upon my recruitment by the University of California, Irvine, in 2003, to found and develop the (only UC system-wide) Institute for Immunology. As the Donald L. Bren Professor of Medicine, Molecular Biology & Biochemistry and Director of the UCI Institute for Immunology, I revamped the Immunology Graduate *curriculum*, obtained an NIH Training Grant in Immunology Research (the first for UCI, NIH T32 AI 060573) for graduate students in 2005, and renewed it in 2010. I left that T32 training grant at UCI upon my recruitment by the University of Texas School of Medicine, Health Science Center at San Antonio (UTHSCSA), on January 1, 2014, as the Zachry Foundation Distinguished Professor and Chairman of the Dept. of Microbiology, Immunology and Molecular Genetics. At UTHSCSA, I have renewed our department commitment and dedication to graduate education by significantly increasing our efforts in the *Infection, Inflammation and Immunity* Discipline of the *Integrated Biomedical Science* (IBMS) Ph.D. program. I have started a new and successful undergraduate research program in partnership with local universities, including Trinity University, Saint Mary University, University of the Incarnate Word, as well as a new and highly successful *Master in Science Program in Immunology and Infection* (45 students in the first two years of existence of the program). I continue to lead a successful research program in B cell biology with emphasis on epigenetics of Ig class switch DNA recombination/somatic hypermutation (CSR/SHM), plasma cell and memory B cell differentiation, as funded by two 5-year NIH R01 grants expiring in 2019 and a 4-year ALR grant expiring in 2019. Because my laboratory performs first-class immunological research with cutting-edge technology and open communication, it provides an environment that enables the next-generation of scientists and physicians to become future leaders in molecular immunology and genetics. I have a passion for teaching and mentoring Ph.D. and M.D./Ph.D. students and postdoctoral fellows. I have received awards for teaching and mentoring excellence from both Cornell University and the University of California. Thus, I have the knowledge, leadership and enthusiasm to successfully mentor one or two students from Xiangya School of Medicine.

**B. Positions and Honors**Positions and Employment

1975-1976 Second Lieutenant and Medical Officer, Italian Army, N.A.T.O. North-East Region [compulsory].

1980-1984 Research Associate ('80-81), Assist. Prof. ('81-84), Department of Immunology, The Scripps Clinic & Research Foundation (currently: The Scripps Research Institute), La Jolla, CA 92037.

1983-1984 Deputy Editor, *The Lancet*, Italian Edition.

1984-1990 Senior Fellow, NIDCR, NIH, U.S. Dept. of Health and Human Services, Bethesda, MD 20892.

1990-1994 Associate Professor of Pathology (tenured), N.Y.U. School of Medicine, New York, NY 10016.

1994-2003 Professor of Pathology and Lab. Medicine (tenured), Cornell University Weill Medical College.

1994-1998 Member, Biology of Aging (Immunology) Review Committee, National Institute of Aging, National Institutes of Health, Bethesda, MD 20892.

1995-2003 Professor of Immunology, Cornell Univ. Weill Grad. School of Med. Sciences, New York, NY 10021.

1997- Adjunct Senior Scientist, Hospital for Special Surgery, New York, NY 10021.

1997-2001 Director, Immunology Graduate Program, Cornell University & Sloan Kettering Weill Graduate School of Medical Sciences, New York, NY 10021.

1998- Member (*ad hoc*) Immunobiology, Immunological Sciences, Allergy & Immunology Study Sections, NIAID, NIAMS, NIA and NCI Special Emphasis Panels, NIH, Bethesda, MD 20892.

1998-2003 Professor of Microbiology & Immunology, Cornell Univ. Weill Med. College, New York, NY 10021.

1998-2003 Co-director, "Host Defense", integrated course of Immunology, Microbiology, Pathology and Principles of Pharmacology, Cornell University Weill Medical College, New York, NY 10021.

1998-2003 Member, Curriculum Committee, Cornell University Weill Medical College, New York, NY 10021.

1999-2003 Member, Committee of Review for Faculty Promotion and Tenure, Basic Sciences and Clinical Series, Cornell University Weill Medical College, New York, NY 10021.

2002- Editor-in-Chief, *Autoimmunity* - Taylor & Francis Publishers, London and New York.  
<http://taylorandfrancis.com/aut>

2003-2013 Donald L. Bren Chair of Medicine, Molecular Biology & Biochemistry, UC Irvine, CA 92697.

2003-2013 Director, *Institute for Immunology*, UC Irvine, CA 92697.

2004-2006 Chairman, IACUC, University of California, Irvine, CA 92697.

2004-2008 Member, HAI Study Section, National Institutes of Health, Bethesda, MD 20892.

2008- Vice-President, *The Institute for Immunobiology*, Baylor College, Houston, TX 77030.

2010-2012 Senior Assoc. Dean for Research and Graduate Studies, School of Medicine, UC Irvine, CA 92697.

2014- Zachry Foundation Distinguished Professor and Chairman, Dept. of Microbiology, Immunology and Molecular Genetics, University of Texas School of Medicine, UT Health Science Center, San Antonio, TX 78229. <http://uthscsa.edu/micro-immunology/>

Other Experience, Professional Memberships and Honors

1975 Fellowship for Scientific and Didactic Formation, University of Milan School of Medicine and Surgery, 20122 Milan, Italy.

1978 *Prix Bizot*, University of Geneva, 1211 Geneva, Switzerland.

1978 *World Health Organization* Field Medical Officer, *All Africa Leprosy Research and Training Center*, *Addis Ababa Leprosy Hospital*, Addis Ababa, Ethiopia.

1981 Member, *American Association of Immunologists*, Bethesda, MD 20814.

1990 *Kaplan Cancer Scholar*, New York University School of Medicine, New York, NY 10116.

1992 Elected "Young Turk", The American Society for Clinical Investigation, Ann Arbor, MI 48103.

2001 Outstanding Teacher Award, Cornell University Weill Medical College, New York, NY 10021.

2002-2005 Counselor, *The Henry Kunkel Society*, The Rockefeller University, New York, NY 10021.

2009 Elected Fellow, *The American Association for Advancement of Science*, Washington, DC 20005.

2011 Recipient, *Athalie Clarke* Research Achievement Award, Irvine, CA 92697.

**C. Contribution to Science**

My research evolved from my early physician activity and clinical investigation stemming from my three experimental theses (experimental theses were then required by the School of Medicine and Surgery of the University of Milan for students wanting to pursue an M.D. *Summa cum Laude* and advanced specializations) in the mid-late '70s to immunochemistry and B cell biology through the '80s, and molecular genetics of antibodies, antibody gene class switch DNA recombination (CSR) and somatic hypermutation (SHM) through the early 2000s, and to this day. I published about 200 articles, many in first class journals. Twenty-five of my publications were cited more than 100 times and 5 more than 400 times. I have been Editor-in-Chief of *Autoimmunity* since 2002. I have authored the Chapter on "DNA recombination and somatic hypermutation in the immune system" in the last three editions (X, XI and XII) of the world renowned *Lewin's GENES* textbook.

**1. Modulation of functions of human lymphocytes, including B cells, by pathogenic viruses.** The profound impact of viruses on the immune system has been long recognized. Clemens Von Pirquet, who is credited with minting the term "allergy", a general a change in body's reactivity, namely in time, quality and quantity (hypersensitivity), showed in 1926 that measles virus infection dampened the immune response to tuberculin in humans. My experiments of the early-mid '80s stemmed from clinical observations of how individuals with flu or other viral infections showed altered responses to vaccines or natural infections. As a postdoctoral fellow at Scripps Clinical and Research Foundation, I showed that measles virus, influenza virus, human cytomegalovirus and Epstein-Barr virus (EBV) modulated specialized, "luxury" functions of human lymphocytes. I showed that glycoproteins that I purified from influenza virus and measles virus induced cytotoxic activity in human NK cells without inducing IFN- $\alpha$  – an important observation, as IFN- $\alpha$  was thought to the necessary mediator for virus or tumor cell-induced cytotoxic activity. I then showed that, contrasting with the function-enhancing activity of viral glycoproteins, whole virions dramatically dampened human lymphocyte functions: cytotoxic activity in T and NK cells and, more profoundly, antibody production in B cells. This was true of measles virus and influenza virus, and only marginally of human cytomegalovirus. By contrast, EBV increased antibody production in human B cells, even before their "immortalization". I detailed the specificity of interaction of EBV with human B cells in elegant experiments in which I biotinylated purified EBV virions and used them with FITC-avidin for analysis in a BD440 FACS machine. Overall, my experiments provided a first and clear understanding of how viruses directly modulate human lymphocyte functions, particularly antibody production, thereby opening a new avenue of research in viral immunobiology.

1. **Casali, P.,** J.G.P. Sissons, M.J. Buchmeier and M.B.A. Oldstone. 1981. Generation of human cytotoxic lymphocytes by virus. Viral glycoproteins induce nonspecific cell mediated cytotoxicity without release of interferon *in vitro*. *J. Exp. Med.* 154:840-855. PMID: [7276828](#); PMCID: [PMC1286447](#).
2. **Casali, P.,** J.G.P. Sissons, R.S. Fujinami and M.B.A. Oldstone. 1981. Purification of measles virus glycoproteins and their integration into artificial lipid membranes. *J. Gen. Virol.* 54:161-172. PMID: [7288404](#).
3. **Casali, P.,** G.P.A. Rice and M.B.A. Oldstone. 1984. Viruses perturb functions of human lymphocyte: Effects of measles virus and influenza virus on lymphocyte mediated killing and antibody production. *J. Exp. Med.* 159:1322-1337. PMID: [6716049](#); PMCID: [PMC2187306](#).
4. Inghirami, G., M. Nakamura, J.E. Balow, A.L. Notkins and **P. Casali**. 1988. Model for studying virus attachment: Identification and quantitation of Epstein-Barr virus-binding cells using biotinylated virus in flow cytometry. *J. Virol.* 62:2453-2463. PMID: [2836625](#); PMCID: [PMC253404](#).

**2. Construction of human mAb-producing cell lines, probing the human B cell repertoire, identification of B1 (B1a and B1b) cells and characterization of "polyreactive" antibodies.** I put to work the knowledge and skills I acquired on the interaction of EBV with B cells to construct human mAb-producing cell lines. This was achieved by adopting a two-step approach, by which EBV-transformed B cells, selected for specificity and isotype, were fused with an Ig-non-secretor human-mouse cell partner to generate stable immortalized B cell lines. This, together with the use of EBV as an one-hit to stimulate human B cells for Ig secretion in limiting dilution analysis allowed for fine probing of the human B cell repertoire specificities and accurate measurement of specific B cell frequencies and dynamics in health and disease. Additionally, these approaches combined with high throughput cell sorting, led to the identification of human B1a (surface Ly1<sup>+</sup>, i.e., CD5<sup>+</sup>) and B1b (surface CD5<sup>-</sup>, mRNA CD5<sup>+</sup>) B cells and their characterization as B lymphocytes that make natural antibodies/autoantibodies, most of which are "polyreactive" – I was responsible for single-handedly forging the term "polyreactive" antibodies in 1987 and for formalizing (with Lee Herzenberg and Randy Hardy) the B1a/B1b cell nomenclature at the New York Academy of Science conference "CD5 B Cells in Development and Disease" in West Palm Beach, 1991.

1. **Casali, P.,** G. Inghirami, M. Nakamura, T.F. Davies and A.L. Notkins. 1986. Human monoclonal antibodies generated by antigen-specific selection of B lymphocytes and transformation by EBV. *Science* 234:476-479. PMID: [3020687](#).
2. **Casali, P.,** S.E. Burastero, M. Nakamura, G. Inghirami and A.L. Notkins. 1987. Human Lymphocytes making rheumatoid factor and antibody to ssDNA belong to the Leu-1<sup>+</sup> B cell subset. *Science* 236:77-81. PMID: [3105056](#).
3. **Casali, P.** and A.L. Notkins. 1989. Probing the human B cell repertoire with Epstein-Barr virus: Polyreactive antibodies and CD5<sup>+</sup> B lymphocytes. *Ann. Rev. Immunol.* 7: 513-535. PMID: [2469441](#).
4. Ueki, Y., I.S. Goldfarb, N. Harindranath, M. Gore, H. Koprowski, A.L. Notkins and **P. Casali**. 1990. Clonal analysis of a human antibody response. Quantitation of precursors of antibody-producing cells and generation and characterization of monoclonal IgM, IgG and IgA to rabies virus. *J. Exp. Med.* 171:19-34. PMID: [2153188](#); PMCID: [PMC2187652](#).



**3. Ig V(D)J gene expression, class-switch DNA recombination (CSR) and somatic hypermutation (SHM) in human B cells in health and disease.** In 1988, Dr. Jim Larrick and I were the first investigators to adapt the PCR to the amplification of expressed Ig genes. By genetic analysis of human mAb-producing cell lines we constructed, we showed that, like neutralizing antibodies to bacteria and viruses, pathogenic autoantibodies, such as lupus anti-double strand DNA IgG, arise from unmutated V(D)J IgM natural antibody templates through CSR/SHM. Analysis of the modalities of SHM led us to identify “inherently hypermutable” codons, such as the V<sub>H</sub> Ser31, which are highly conserved in human and mouse V genes. It also led us to identify the IgH chain CDR3 as the major structural correlate of antigen binding in natural polyreactive antibodies. Further, it provided impetus for systematically pursuing the molecular mechanisms underpinning CSR/SHM. In this line of research, we defined roles for translesion DNA synthesis polymerase  $\zeta$  (Rev3) and polymerase  $\theta$ , as well as elements of the DNA MMR repair machinery, particularly Mlh3, in SHM. We also outlined a scaffold (non-enzymatic) role for lesion bypass DNA polymerase Rev1 in CSR. Finally, we demonstrated the central role of the homologous recombination Rad52 element in mediating alternative NHEJ in CSR by competing with Ku70/86 for binding to S region DNA double-strand break ends (H. Zan, C. Tat, Z. Qiu, J.R. Taylor, J. Guerrero, T. Shen & P. Casali. 2017. *Nature Commun.* 8:14244 DOI:10.1038/ncomms14244).

1. Ichiyoshi, Y. and **P. Casali**. 1994. Analysis of the structural correlates for antibody polyreactivity by multiple reassortments of chimeric human immunoglobulin heavy and light chain V segments. *J. Exp. Med.* 180:885-895. PMID: [8064239](#); PMCID: [PMC2191637](#).
2. Zan, H., A. Komori, Z. Li, A. Cerutti, M. Flajnik, M. Diaz and **P. Casali**. 2001. The translesion DNA polymerase  $\theta$  plays a major role in immunoglobulin and Bcl-6 somatic hypermutation. *Immunity* 14:643-653. PMID: [11371365](#); PMCID: [PMC4632985](#).
3. Zan, H., X. Wu, A. Komori, A. Cerutti, W.K. Holloman and **P. Casali**. 2003. AID-dependent generation of resected double-strand DNA breaks and recruitment of Rad52/Rad51 in somatic hypermutation. *Immunity* 18:727-738. PMID: [12818155](#); PMCID: [PMC4625537](#).
4. Zan, H., C.A. White, L.M. Thomas, T. Mai, G. Li, Z. Xu, J. Zhang and **P. Casali**. 2012. Rev1 recruits Ung to switch regions and enhances dU glycosylation for immunoglobulin class switch DNA recombination. *Cell Rep.* 2:1220-1232. PMID: [23140944](#); PMCID: [PMC3518390](#).

**4. Defining the stimuli, modalities of signal transduction and function of transcription factors in induction and modulation of AID expression and CSR/SHM.** Starting in 2000, we mounted a systematic effort to address stimuli and signaling underpinning B cell *Aicda* expression and CSR/SHM in immunity, autoimmunity and lymphomagenesis. By devising new tools, such as the first monoclonal human IgM<sup>+</sup>IgD<sup>+</sup>B cell line that can be induced *in vitro* to undergo high rates of CSR/SHM and by significantly improving existing technologies, we have defined the induction of CSR/SHM by engagement of CD40 in T cell-dependent antibody responses and dual engagement of a TLR and BCR in T cell-independent antibody responses. We have also addressed regulation of CSR/SHM induction by ligands of other receptors in B cells, including CD30, which engages CD153, and BAFF, as produced by different immune cells; this led to addressing the dysregulation in CD153 signaling and AID activity in B cell lymphomagenesis. Partially building on these findings, we have recently identified a role of intracellular membrane structures in signal transduction in B cell differentiation, as exemplified by Rab7, a small GTPase that promotes the formation of mature endosomes, in mediating T-dependent and T-independent CSR and antibody responses. Rab7 does so by promoting expression of AID through activation of transcription factor NF- $\kappa$ B. NF- $\kappa$ B, as we have shown, synergizes with the HoxC4 homeodomain transcription factor to activate the *Aicda* gene promoter in human and mouse B cells, thereby critically mediating induction of AID. These findings are informing our analysis of the dysregulation of Rab7, HoxC4 and AID by estrogen in lupus B cells, as derived from patients and lupus mouse models.

1. Cerutti, A., A. Schaffer, S. Shah, H. Zan, H.C. Liou, R.G. Goodwin and **P. Casali**. 1998. CD30 is a CD40-inducible molecule that negatively regulates CD30-mediated immunoglobulin class switching in non-antigen-selected human B cells. *Immunity* 9: 239-246, 1998. PMID: [9729045](#); PMCID: [PMC4621001](#).
2. Park, S.-R., H. Zan, J. Zhang, A. Al-Qahtani, E.J. Pone, Z. Xu, T. Mai and **P. Casali**. 2009. HoxC4 binds to the promoter of the cytidine deaminase AID gene to induce AID expression, immunoglobulin class switch DNA recombination and somatic hypermutation. *Nature Immunol.* 10: 540-550. PMID: [19363484](#); PMCID: [PMC2753990](#).
3. Pone, E.J., J. Zhang, T. Mai, C.A. White, G. Li, P. Patel, A. Al-Qahtani, J. Sakakura, H. Zan, Z. Xu and **P. Casali**. 2012. BCR-signalling synergizes with TLR-signalling for induction of AID and immunoglobulin class switch DNA recombination through the non-canonical NF- $\kappa$ B pathway. *Nature Comm.* 3: 767:1-12. PMID: [22473011](#); PMCID: [PMC3337981](#).
4. Pone E. J., T. Lam, Z. Lou, R. Wang, Y. Chen, D.F. Liu, A. L. Edinger, Z. Xu and **P. Casali**. 2015. B cell Rab7 mediates induction of AID expression and class-switching in T-dependent and T-independent antibody responses. *J. Immunol.* 194: 3065-3078. PMID: [25740947](#); PMCID: [PMC4643723](#).

**5. Epigenetics of B cell differentiation and the antibody response.** Recently, we have committed significant resources to investigate the role of epigenetics, particularly, histone posttranslational modifications and non-coding RNAs, including microRNAs, in targeting and regulating the B cell CSR/SHM machinery and plasma cell differentiation. Targeting of the CSR machinery, including the potentially genotoxic AID, to switch (S) region DNA in the *IgH* locus is critical for CSR to unfold and to avoid genome-wide DNA damage. We have shown that S regions are rich in 5'-AGCT-3' motifs and undergo acetylation of histone H3K9 acetylation/S10 phosphorylation (H3K9acS10ph) upon induction of CSR. We have identified 14-3-3 proteins as adaptors that simultaneously bind 5'-AGCT-3' repeats and H3K9acS10ph with high affinity. Upon binding to S region DNA and posttranslational modified histones, 14-3-3 proteins in turn stabilize AID onto the same S regions. Expression of 14-3-3 $\gamma$  and AID is under direct regulation of epigenetic marks, e.g., histone modifications in the 14-3-3 $\gamma$  gene promoter and microRNAs that target the 3'-UTR of the *Aicda* mRNA transcripts. Using high-throughput analysis of the transcriptome and miRNome, we have shown that HDAC (histone deacetylase) inhibitors (HDIs) specifically downregulate expression of AID and Blimp-1 (master transcription factor of plasma cell differentiation) by upregulating microRNAs that target *Aicda* or *Prdm1* (encoding Blimp-1) 3'-UTR. These specific epigenetic changes effectively modulate CSR/SHM and antibody responses. They also blunt autoantibody responses in lupus-prone mice, thereby alleviating lupus immunopathology, and outlining an important role of epigenetic modifications in the regulation of B cell differentiation in autoimmunity.

1. Xu, Z., Z. Fulop, G. Wu, E. J. Pone, J. Zhang, T. Mai, L. Thomas, A. Al-Qahtani, C.A. White, S.-R. Park, P. Steinacker, Z. Li, J. R. Yates, III, B. Herron, M. Otto, H. Zan, H. Fu and **P. Casali**. 2010. 14-3-3 adaptor proteins recruit AID to 5'-AGCT-3'-rich switch regions for class switch DNA recombination. *Nature Struct. Mol. Biol.* 17: 1124-1135. PMID: [20729863](#); PMCID: [PMC3645988](#).
2. Li, G., C.A. White, T.S. Lam, E.J. Pone, D.C. Tran, K.L. Hayama, H. Zan, Z. Xu and **P. Casali**. 2013. Combinatorial H3K9acS10ph histone modifications in *IgH* locus switch regions target 14-3-3 adaptors and AID to specify antibody class switch DNA recombination. *Cell Rep.* 5:702-714. PMID: [24209747](#); PMCID: [PMC3951903](#).
3. White, C.A., E.J. Pone, T. Lam, C. Tat, K.L. Hayama, G. Li, H. Zan and **P. Casali**. 2014. Histone deacetylase inhibitors upregulate B cell microRNAs that silence AID and Blimp-1 expression for epigenetic modulation of antibody and autoantibody responses. *J. Immunol.* 193: 5933-5950. PMID: [25392531](#); PMCID: [PMC4258531](#).
4. Shen, T., H.N. Sanchez, H. Zan and **P. Casali**. 2015. Genome-wide analysis reveals selective modulation of microRNAs and mRNAs by histone deacetylase inhibitor in B cells induced to undergo class-switch DNA recombination and plasma cell differentiation. *Front. Immunol.* PMID: [26697020](#); PMCID: [PMC4677488](#).

#### Complete List of Published Work in My Bibliography (200 publications):

<http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40448339/?sort=date&direction=ascending>

#### D. Research Support

##### Ongoing Research Support:

NIH R01 AI 079705

12/01/2014 - 11/31/2019.

P.I.: Paolo Casali

*Rab7 and Estrogen-ER $\alpha$  as B cell-intrinsic mediators of antibody/autoantibody responses.*

The goal of this project is to delineate the role of cytoplasmic membrane Rab7 and ER- $\alpha$  in modulating class switch DNA recombination, somatic hypermutation and plasmacytoid B cell differentiation.

NIH R01 AI 105813

02/01/2014 - 01/31/2019.

P.I.: Paolo Casali

*Epigenetic modulation of antibody and autoantibody responses.*

The goal of this project is to outline the role of histone posttranslational modifications and non-coding RNAs in class switch DNA recombination, somatic hypermutation and plasma cell differentiation.

Alliance for Lupus Research D 257547

02/01/2014 - 01/31/2018.

P.I.: Paolo Casali

*B cell histone posttranslational modifications and non-coding RNAs as therapeutic targets in lupus.*

The goal of this project is to identify effective as therapeutic targets in lupus B cells.

NIH R01 AI 105813-S1

08/01/2016 - 07/31/2020.

P.I.: Paolo Casali

*TLR-mediated epigenetic modulation of the antibody response. Research Supplements to Promote Diversity in Health-Related Research.*

The goal of this project is to outline the role of TLR-signaling in epigenetic modulation of class switch DNA recombination, somatic hypermutation and plasma cell differentiation.

**Pending Research Support:**

NIH T32 AI 125208	07/01/2018- 06/31/2023	\$126,320
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P.I.: Paolo Casali

*Graduate Research in Immunology and Infection Program (GRIIP): to train graduate students for successful careers in academia, industry and government.*

The goal of this project is to train graduate students for successful careers in academia, industry and government by taking advantage of the biomedical research enterprise and clinical settings of the University of Texas Health Science at San Antonio.

**Paolo Casali, M.D.****RESEARCH SUPPORT (COMPLETE INFORMATION):** Funding Period Current/First Year Direct Costs**Ongoing Research Support**

NIH R01 AI 079705	12/01/2014 - 11/30/2019	\$327,243
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Principal Investigator: Paolo Casali [score: 1.0]

*Estrogen-ER $\alpha$  and Rab7 as B cell -intrinsic mediators of antibody and autoantibody responses.*

NIH R01 AI 105813	02/01/2014 - 11/31/2019	\$332,721
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Principal Investigator: Paolo Casali [score: 1.0]

*Epigenetic downregulation of the antibody response and inhibition of autoimmunity.*

Alliance for Lupus Research ID 257547	02/01/2014 - 01/31/2018	\$200,000
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Principal Investigator: Paolo Casali

*HDAC inhibitors and B cell microRNAs in lupus therapy.*

NIH AI 105813-03S1	09/01/2016 – 01/31/2019	\$33,646
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Principal Investigator: Paolo Casali [score: N/A]

*Diversity Supplement Epigenetic downregulation of the antibody and autoantibody response.*

**Pending Research Support**

NIH T32 AI 125208	07/01/2017- 06/31/2022	\$126,320
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Principal Investigator: Paolo Casali

*Graduate Research in Immunology and Infection Program (GRIIP): to train graduate students for successful careers in academia, industry and government.*

**Completed Research Support (last 3 years)**

NIH 5T32 AI 060573	08/01/2005- 06/31/2015	\$116,320
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Principal Investigator: Paolo Casali

*Immunology Research Training Program.*

This NIH grant was left behind at UCI by Dr. Casali as of 01/01/2014.

NIH R01 AI 045011/R56 AI 045011-01	08/01/2009 - 07/31/2014	\$522,558
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Principal Investigator: Paolo Casali [score: 1.2]

*Immunoglobulin class switch DNA recombination.*

## **Description of the Project: Microbiology, Immunology and Molecular Genetics (MIMG)**

Xiangya students for the 2017-2019 period will work on the following:

Regulation of antibody gene expression, class-switch DNA recombination, somatic hyper mutation, epigenetics (microRNAs, long non-coding RNAs, HDACs HADAC inhibitors, including metabolic by-products by microbiota) of the antibody response and mechanisms of generation of memory B cells and plasma cells in vitro and in vivo (mouse and human) using cutting edge technologies and experimental approaches, including humanized mice, next generation sequencing, CRISPR/Cas9 gene editing and a variety of genetically modified mice.